

Supplemental Data

Supplemental Table 1. Summary of Adverse Events

Adverse Events	Subjects (N = 16)	
	Advate Treatment Period	rFVIIIFc Treatment/Follow-up Period
Total Number of Adverse Events	6	44
Number of Subjects with at least one AE	5	11
Lymphadenopathy	0	1
Tachycardia	0	1
Ear disorder	0	1
Photophobia	0	1
Nausea	0	1
Application site vesicles	0	1
Fatigue	0	1
Injection site edema	1	0
Malaise	0	1
Allergy to plants	1	1
Nasopharyngitis	0	3
Upper respiratory infection	0	1
Blood potassium decreased	0	1
Arthralgia	0	1
Back pain	0	2
Hemophilic arthropathy	1	1
Muscle tightness	0	1
Musculoskeletal chest pain	0	1
Myalgia	1	2
Neck pain	0	1
Pain in extremity	1	0
Dizziness	1	1
Dysguesia	0	2
Headache	0	3
Hyperreflexia	0	1
Paresthesia	0	1

Disorientation	0	1
Insomnia	0	1
Nasal congestion	0	1
Oropharyngeal pain	0	1
Ecchymosis	0	1
Flushing	0	1
Hypertension	0	1

Supplemental Table 2. PK Parameters by Two-Stage (Chromogenic) Assay for rFVIIIFc and Advate Per Dose Group

Parameter	Dose: 25 IU/kg (N=6)			Dose: 65 IU/kg (N=9)		
	Advate Geom. Mean [95% CI]	rFVIIIFc Geom. Mean [95% CI]	Geom. Mean Ratio [95% CI] (p-value)	Advate Geom. Mean [95% CI]	rFVIIIFc Geom. Mean [95% CI]	Geom. Mean Ratio [95% CI] (p-value)
C_{max} (IU/dL)	75.5 [65.5, 87.1]	76.5 [64.9, 90.1]	1.01 [0.940, 1.09] (p = 0.686)	175 [143, 215]	182 [146, 227]	1.04 [0.900, 1.20] (p = 0.571)
AUC_{INF} (hr*IU/dL)	1060 [822, 1360]	1660 [1300, 2120]	1.57 [1.38, 1.80] (p < 0.001)	2270 [1670, 3070]	4280 [2960, 6190]	1.89 [1.61, 2.21] (p < 0.001)
t_{1/2} (hr)	10.5 [8.49, 12.9]	16.7 [13.8, 20.1]	1.59 [1.35, 1.87] (p < 0.001)	10.8 [8.16, 14.2]	19.8 [14.3, 27.5]	1.84 [1.60, 2.12] (p < 0.001)
MRT (hr)	15.0 [12.2, 18.6]	23.9 [19.8, 28.9]	1.59 [1.35, 1.87] (p < 0.001)	15.4 [11.7, 20.4]	28.5 [20.5, 39.6]	1.85 [1.61, 2.12] (p < 0.001)
CL (mL/hour/kg)	2.35 [1.80, 3.06]	1.49 [1.16, 1.92]	0.636 [0.557, 0.727] (p < 0.001)	2.87 [2.12, 3.89]	1.52 [1.05, 2.20]	0.530 [0.453, 0.620] (p < 0.001)
V_{ss} (mL/kg)	35.5 [30.5, 41.3]	35.9 [30.4, 42.3]	1.01 [0.898, 1.14] (p = 0.822)	44.5 [36.7, 54.1]	43.4 [38.2, 49.4]	0.975 [0.863, 1.10] (p = 0.653)
Incremental Recovery (IU/dL per IU/kg)	3.05 [2.62, 3.54]	3.09 [2.61, 3.66]	1.01 [0.940, 1.09] (p = 0.679)	2.70 [2.20, 3.31]	2.80 [2.24, 3.50]	1.04 [0.900, 1.20] (p = 0.571)

Supplemental Figure 1. Correlation of rFVIII Activity by One-Stage (aPTT) and Chromogenic Assays

Correlation between one-stage clotting (aPTT) and chromogenic assay results measuring FVIII activity (IU/mL) following injection of Advate (♦) and rFVIIIFc (□)

